STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 120158

TO: David Lukton Location: REM/3B75/3C70 Art Unit: 1653 April 23, 2004 Case Serial Number: 09/868395	From: P. Sheppard Location: Remsen Building Phone: (571) 272-2529 sheppard@uspto.gov

Search Notes

Access DB# 120158

SEARCH REQUEST FORM
(STIC)

Requestor's Name: David Lukton   Examiner number: 71263   Date: 04-22-04

Art Unit: 1653   Phone number: 571-272-0952   Serial Number: 09-868395

Mail Box: 3-C-70   Examiner Rm: 3-B-75   Results format: paper

* * * * * * * * * * * * * *

Title of Invention: Compounds useful in the treatment of inflammatory diseases

Applicants: ARMOUR, DUNCAN ROBERT; BROWN, DAVID; CONGREVE, MILES; GORE, PAUL MARTIN; GREEN, DARREN VICTOR STEVEN; HOLMAN, STUART; JACK, TORQUIL IAIN MACLEAN; KEELING, STEVEN PHILIP; MASON, ANDREW MCMURTRIE; MORRISS, KAREN; RAMSDEN, NIGEL GRAHAME; WARD, PETER

Earliest Priority Date: 12/18/98

* * * *

Applicants are claiming compounds on the attached sheet.

R^1 = anything that contains at least one carbon atom

R^2 = anything that contains at least one carbon atom

R^6 = hydrogen, or R^6 forms a pyrrolidine ring with R^4

R^4 = anything; or R^4 forms a pyrrolidine ring with R^6

R^{10} is any of the following:

$C_6H_5\text{-}(CH_2)_n\text{-}CO\text{-}$ n = 0, 1, 2

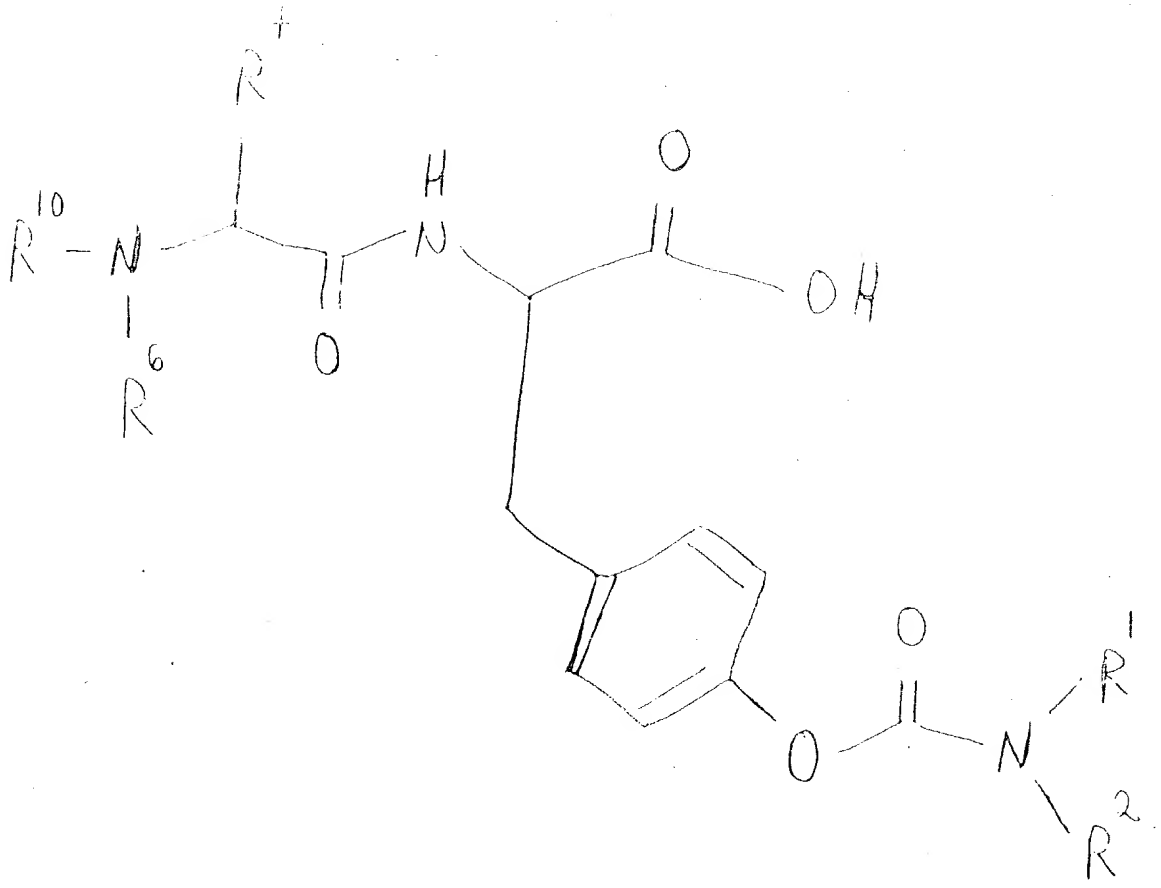
$H_2N\text{-}CH(R^8)\text{-}CO\text{-}$ R^8 = hydrogen or alkyl

$C_6H_5\text{-}CH_2\text{-}O\text{-}CO\text{-}$

****

STAFF USE ONLY   **Type of Search**   **Vendors and cost where applicable**

09/868395



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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
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FILE COVERS 1907 - 23 Apr 2004  VOL 140 ISS 18
FILE LAST UPDATED: 22 Apr 2004  (20040422/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


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L3                STR
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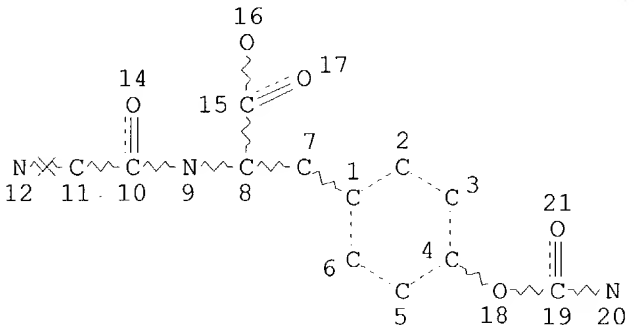


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DEFAULT ECLEVEL IS LIMITED

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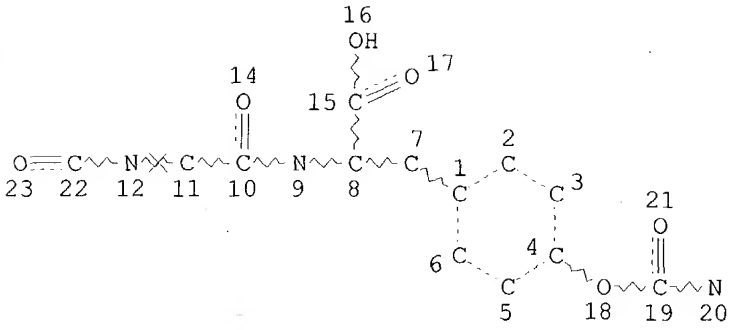

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DEFAULT ECLEVEL IS LIMITED

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NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
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L12 2 SEA FILE=HCAPLUS ABB=ON PLU=ON L11

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=> d ibib abs hitrn l12 1-2

L12 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:513715 HCAPLUS
DOCUMENT NUMBER: 133:129864
TITLE: Pyroglutamic acid derivatives and related compounds which inhibit leukocyte adhesion mediated by VLA-4, and preparation thereof
INVENTOR(S): Dressen, Darren B.; Kreft, Anthony; Kubrak, Dennis; Mann, Charles William; Pleiss, Michael A.; Stack, Gary Paul; Thorsett, Eugene D.
PATENT ASSIGNEE(S): Elan Pharmaceuticals, Inc., USA; American Home Products Corporation
SOURCE: PCT Int. Appl., 187 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000043413	A2	20000727	WO 2000-US1537	20000121
WO 2000043413	A3	20001130		

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2358093	AA	20000727	CA 2000-2358093	20000121
EP 1144435	A2	20011017	EP 2000-904486	20000121
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US 6407066	B1	20020618	US 2000-489164	20000121
US 2003027771	A1	20030206	US 2002-139382	20020507

PRIORITY APPLN. INFO.:	US 1999-198244P	P	19990126
	US 1999-238661	A1	19990126
	US 2000-489164	A1	20000121
	WO 2000-US1537	W	20000121

OTHER SOURCE(S): MARPAT 133:129864

AB Pyroglutamic acid derivs. and related compds. that bind VLA-4 are disclosed. Certain of these compds. also inhibit leukocyte adhesion and, in particular, leukocyte adhesion mediated by VLA-4. Such compds. are useful in the treatment of inflammatory diseases in a mammalian patient, e.g., human, such as asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, rheumatoid arthritis, tissue transplantation, tumor metastasis, and myocardial ischemia. The compds. can also be administered for the treatment of inflammatory brain diseases such as multiple sclerosis.

IT **286456-80-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pyroglutamic acid derivs. and related compds. which inhibit VLA-4-mediated leukocyte adhesion, and prepn. thereof)

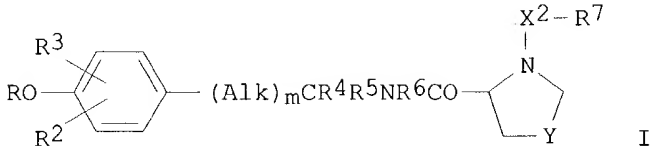
L12 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	1998:795039 HCAPLUS
DOCUMENT NUMBER:	130:52733
TITLE:	Preparation of tyrosine derivatives as antiinflammatory agents
INVENTOR(S):	Head, John Clifford; Archibald, Sarah Catherine; Warrellow, Graham John
PATENT ASSIGNEE(S):	Celltech Therapeutics Limited, UK
SOURCE:	PCT Int. Appl., 55 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9854207	A1	19981203	WO 1998-GB1580	19980529
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9876674	A1	19981230	AU 1998-76674	19980529
EP 984981	A1	20000315	EP 1998-924481	19980529
EP 984981	B1	20031217		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6093696	A	20000725	US 1998-86421	19980529
JP 2002501518	T2	20020115	JP 1999-500393	19980529

AT 256699 E 20040115 AT 1998-924481 19980529
PRIORITY APPLN. INFO.: GB 1997-11143 A 19970530
GB 1997-22674 A 19971027
WO 1998-GB1580 W 19980529
OTHER SOURCE(S): MARPAT 130:52733
GI



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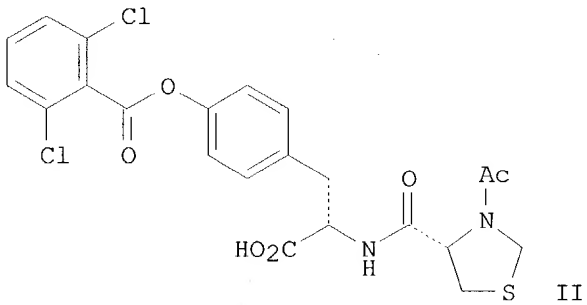

II

AB Tyrosine derivs. I [R = R1X1, (Hal1)3CSO2; R1 = optionally substituted alkyl or arom. group; R2, R3 = independently H, halo, alkyl, alkoxy, OH, NO2; R4 = H, Me; R5 = (CH2)pCO2R8; R6= H, alkyl; R7 = optionally substituted alkyl group, aryl, aralkyl; R8 = H, alkyl; Alk = alkylene chain; Hal1 = F, Cl; X1 = bond, (CH2)n, CO, CH2CO, NHCO, CH2NHCO, SO2; X2 = CO, CO2, CONH, SO2; Y = S, S(O)q; m = 0, 1; n = 1, 2; p = 0, 1; q = 1, 2] and the salts, solvates and hydrates thereof, are described. The compds. are able to inhibit the binding of .alpha.4 integrins to their ligands and are of use in the prophylaxis and treatment of immune or inflammatory disorders. Thus, coupling of N-acetyl-D-thioproline with L-tyrosine tert-Bu ester, followed by O-acylation with 2,6-dichlorobenzoyl chloride and acidic deesterification, gave desired tyrosine deriv. II. II and related thioprolyltyrosine derivs. were tested for inhibition of .alpha.4 integrin-dependent cell adhesion, and generally have IC50 values of .ltoreq.1 .mu.M in .alpha.4.beta.1 and .alpha.4.beta.7 assays, and IC50 values of .gtoreq. 50 .mu.M in assays of other integrins.

IT **217479-20-4P 217479-30-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of tyrosine derivs. as antiinflammatory agents)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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=> fil caold
FILE 'CAOLD' ENTERED AT 14:07:35 ON 23 APR 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

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L13 0 L11

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=> fil reg
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USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 21 APR 2004 HIGHEST RN 676437-01-7
DICTIONARY FILE UPDATES: 21 APR 2004 HIGHEST RN 676437-01-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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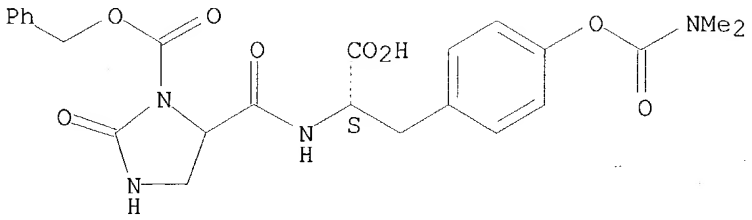
L11 ANSWER 1 OF 3 REGISTRY
RN 286456-80-2 REGISTRY
CN 1-Imidazolidinecarboxylic acid, 5-[[[(1S)-1-carboxy-2-[4-[[(dimethylamino)carbonyl]oxy]phenyl]ethyl]amino]carbonyl]-2-oxo-, 1-(phenylmethyl) ester (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H26 N4 O8
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



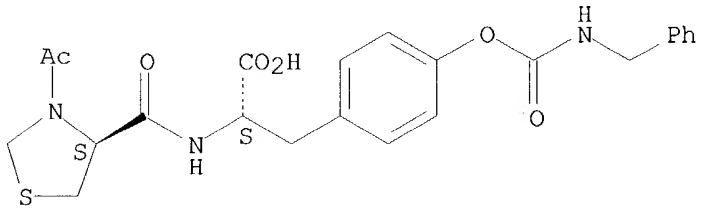
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 133:129864

L11 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN
RN 217479-30-6 REGISTRY
CN L-Tyrosine, N-[[(4S)-3-acetyl-4-thiazolidinyl]carbonyl]-, (phenylmethyl)carbamate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H25 N3 O6 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



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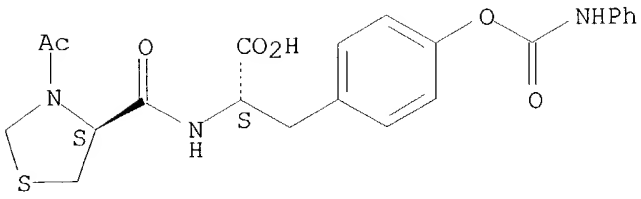
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 130:52733

L11 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN
RN 217479-20-4 REGISTRY
CN L-Tyrosine, N-[[(4S)-3-acetyl-4-thiazolidinyl]carbonyl]-, phenylcarbamate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C22 H23 N3 O6 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 130:52733

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FILE COVERS 1907 - 23 Apr 2004  VOL 140 ISS 18
FILE LAST UPDATED: 22 Apr 2004  (20040422/ED)

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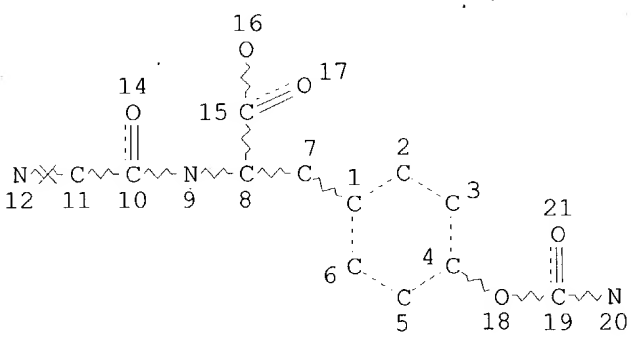


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NUMBER OF NODES IS  20

STEREO ATTRIBUTES: NONE
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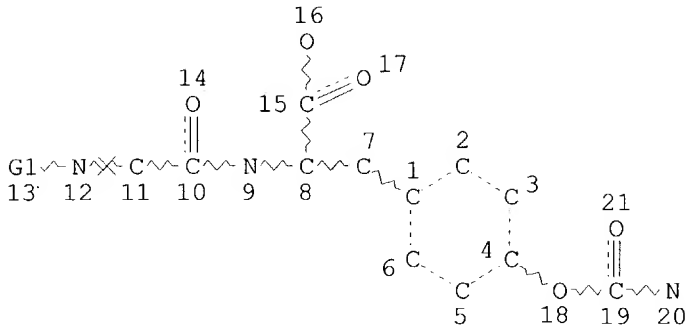

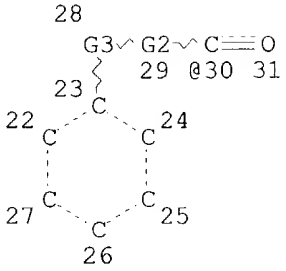

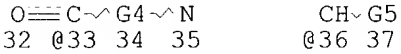

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REP G3=(0-2) C
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DEFAULT ECLEVEL IS LIMITED

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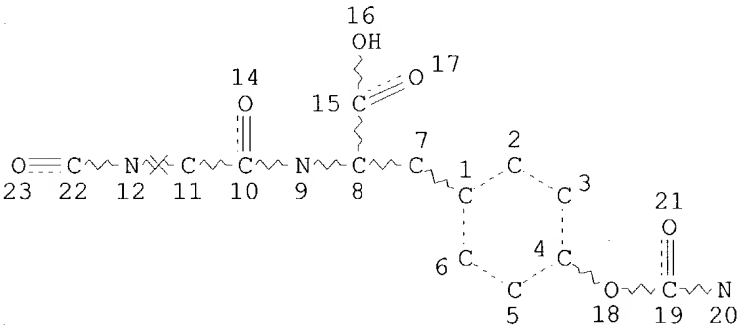
L10 STR



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STEREO ATTRIBUTES: NONE
L11 3 SEA FILE=REGISTRY SUB=L5 SSS FUL L10

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L14             7 SEA FILE=REGISTRY ABB=ON  PLU=ON  L7 NOT L11
L15             5 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L14 NOT L12


=>
=>

=> d ibib abs hitrn l15 1-5

L15  ANSWER 1 OF 5  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         1990:578192  HCAPLUS
DOCUMENT NUMBER:          113:178192
TITLE:                    Biomaterials based on "pseudo"-poly(amino acids):  a
                          study of tyrosine-derived polyiminocarbonates
AUTHOR(S):                Pulapura, S.; Kohn, J.
CORPORATE SOURCE:         Dep. Chem., Rutgers Univ., New Brunswick, NJ, 08855,
                          USA
SOURCE:                   Polymer Preprints (American Chemical Society, Division
                          of Polymer Chemistry) (1990), 31(1), 233-4
                          CODEN: ACPPAY; ISSN: 0032-3934
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
GI
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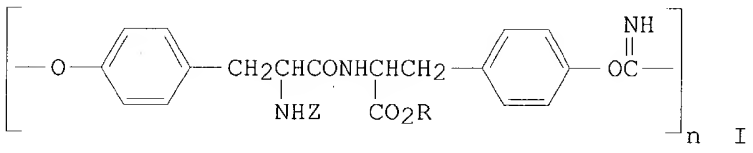

I

AB Polyiminocarbonates, e.g. I (R = Et, hexyl, or palmityl) were prepd. and their properties detd. Incorporation of nonamide linkages into the backbone of the poly(amino acids) leads to an improvement of the processibility and the physicomech. properties of the polymers. None of the polymers exhibited gross toxicity or tissue incompatibility on s.c. implantation in mice, rats, or rabbits.

IT **106231-87-2P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and properties of, for biomaterials)

```
L15  ANSWER 2 OF 5  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         1989:595409  HCAPLUS
DOCUMENT NUMBER:          111:195409
TITLE:                    Preparation of nonpeptide polyamino acid bioerodible
                          polymers for drug formulations
INVENTOR(S):              Kohn, Joachim; Langer, Robert S.
PATENT ASSIGNEE(S):       Massachusetts Institute of Technology, USA
SOURCE:                   U.S., 9 pp.
                          CODEN: USXXAM
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
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     US 4638045         A    19870120      US 1985-703153   19850219
     US 4863735         A    19890905      US 1986-914380   19861002
PRIORITY APPLN. INFO.:                  US 1985-703153      19850219
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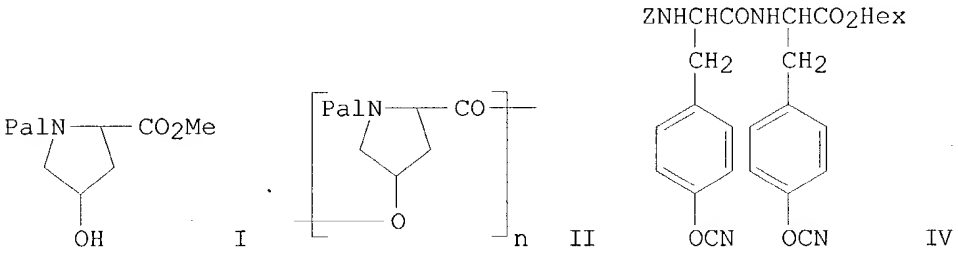
AB Biodegradable polymers are prepd. by polymn. of ZNHCHR1CONHCHR2COY or ZNHCHR1CONHCHR2CONHCHR3COY (R1-R3 = side chains of L-.alpha.-amino acids; Y, Z = protecting group) through .gtoreq.1 of R1-R3, useful for controlled release applications in vivo and vitro for delivery of a wide variety of biol. and pharmacol. active ligands. are prepd. Thus, Z-Glu-Phe-OH (Z = PhCH2O2C) and Et3N in CH2Cl2 were treated with (PhO)2P(O)Cl and the mixt. was kept at 4.degree. for 12 h to give a polymer with an av. mol. wt. of 17,000.

IT **123375-14-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as bioerodible material)

L15 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1987:67663 HCAPLUS
DOCUMENT NUMBER: 106:67663
TITLE: Polymerization reactions involving the side chains of .alpha.-L-amino acids
AUTHOR(S): Kohn, Joachim; Langer, Robert
CORPORATE SOURCE: Dep. Appl. Biol. Sci., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SOURCE: Journal of the American Chemical Society (1987), 109(3), 817-20
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 106:67663
GI



AB Hydroxyproline deriv. I (Pal = palmitoyl) underwent melt transesterification in the presence of Al isopropoxide to give side-chain polymer II. Z-Tyr-Tyr-OHex (III; Z = PhCH2O2C, Hex = hexyl) was treated with cyanogen bromide to give dicyanate IV. The soln. polymn. of equimolar amts. of III and IV in THF contg. KOCMe3 gave the corresponding iminocarbonate side-chain polymer.

IT **106231-87-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L15 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1970:510135 HCAPLUS
DOCUMENT NUMBER: 73:110135
TITLE: Tyrosine-containing peptides and their pharmaceutical preparations
PATENT ASSIGNEE(S): Farbwerke Hoechst A.-G.
SOURCE: Brit., 11 pp.
CODEN: BRXXAA
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 1201121		19700805		
DE 1593858			DE	
DE 1643327			DE	
US 3538070		19700000	US	

PRIORITY APPLN. INFO.: DE 19670302
DE 19670707

AB The title peptides are useful in the synthesis of peptides with ACTH-like activity, and insulin, glucagon, and hypertensin. In this abstr., For = formyl, Z = carbobenzoxy, ONP = 4-nitrophenyl, BOC = tert-butoxycarbonyl, TCP = 2,4,5-trichlorophenyl, MeOC = methoxycarbonyl, PrOC = isopropoxycarbonyl, BuOC = isobutoxycarbonyl, EtOC = ethoxycarbonyl, AC = carbamoyl, BAC = isobutylcarbamoyl, PAC = phenylcarbamoyl, NPAC = 4-nitrophenylcarbamoyl, and all amino acids are of the L-series. To 31.5 g Z-Tyr-OH in 150 ml N NaOH was added 15 g Na2CO3 and 11 ml ClCO2Et to give 36.1 g Z-Tyr-(EtOC)-OH (I), m. 117-19.degree. (MeOH). Similarly were prepd.: Z-Tyr-(BuOC)-OH, 103-5.degree.; Z-Tyr-(MeOC)-OH, m. 120-2.degree.; Z-Tyr-(PrOC)-OH, 119-21.5.degree.; and BOC-Tyr-(EtOC)-OH, m. 165-6.degree.. To 7.74 g I and 3.34 g 4-O2NC6H4OH in 70 ml AcOEt and 30 ml DMF at 0.degree. was added 4.2 g dicyclohexylcarbodiimide (Ia) to give 6.28 g Z-Tyr-(EtOC)-ONP (II), m. 111-12.degree. (iso-PrOH). H-Phe-OMe.HCl (1.08 g), 2.54 g II, 15 ml DMF, and 0.69 ml Et3N gave 2.4 g Z-Tyr-(EtOC)-Phe-OMe (III), m. 176-6.5.degree. (aq. MeOH). Treatment of 4.79 g Z-Tyr-Phe-OMe in 25 ml THF and 60 ml CHCl3 with 1.67 ml Et3N followed by 1.09 ml ClCO2Et also gave III. III (1.37 g) 0.95 ml 80% N2H4.H2O, and 100 ml MeOH gave 0.97 g Z-Tyr-Phe-NHNH2, m. 241-5.degree. (80% MeOH). Z-Tyr-OMe (IIIa) (6.6 g) in 50 ml CHCl3 with 3.22 ml Et3N and 2.17 ml ClCO2Et at 0.degree. gave 6.5 g Z-Tyr-(EtOC)-OMe, m. 95-5.5.degree. (iso-Pr2O) which (4.01 g) on hydrogenation in 100 ml MeOH and 2.09 ml 4.97 N HCl in the presence of Pd gave 1.9 g H-Tyr-(EtOC)-OMe.HCl (IV), m. 162-3.degree.. Similarly, 1.49 g Z-Phe-OH in 15 ml THF with 0.7 ml Et3N and 0.48 ml ClCO2 Et and addn. of 1.52 g IV in 20 ml Me2NAc contg. 0.7 ml Et3N gave 1.88 g Z-Phe-Tyr-(EtOC)-OMe, m. 170.5-1.5.degree., which with N NaOH at room temp. gave Z-Phe-Tyr-OH, m. 181.5-83.degree.. For-Tyr-(EtOC)-OH (V), m. 172-3.degree. (25% MeOH), was prepd. in 81.5% yield from For-tyr-OH and ClCO2Et in N NaOH. A soln. of 7 g BOC-Ser-Met-OMe in 54 ml methanolic 0.55N HCl was kept 1 hr at room temp. to remove the BOC group and the product in 40 ml 1:1 MeCNMe2NAc treated with 2.81 ml Et3N, 5.62 g V, and 4.3 g Ia at -5.degree. to give 7.6 g For-Tyr-(EtOC)-Ser-Met-OMe (VI), m. 164-6.degree. (AcOEt). Treatment of VI in MeOH with N2H4.H2O at room temp. gave For-Tyr-Ser-Met-NHNH2, m. 208-10.degree. (80% MeOH), in 74% yield. To 7.7 g I and 2.8 ml Et3N in 40 ml THF was added 2.6 ml ClCO2Bu-iso at -5.degree. followed after 10 min by 3.73 g H-Gly-NH2.HCl and 4 ml Et3N in a little H2O, to give 8.08 g Z-Tyr-(EtOC)-Gly-NH2 (VII), m. 157-9.degree. (MeCOEt). Treatment of 4.43 g VII with 40 ml methanolic 2N NH3 gave 3.42 g Z-Tyr-Gly-NH2, m. 114-16.degree.. A mixt. of 3.53 g BOC-Tyr-(EtOC)-OH and 50 ml AcOEt satd. with HCl pptd. H-Tyr-(EtOC)-OH.HCl, m. 219-20.degree. (decompn.), from which H-Tyr-(EtOC)-OH was obtained by treatment with hot 10% aq. C5H5N. To 3.29 g IIIa in 4 ml MeCN was added 0.89 ml N-carbonylsulfamoyl chloride to give 1.75 g Z-Tyr-(AC)-OMe (VIII), m. 131.5-32.degree. (CHCl3-Et2O). VIII was also prepd. by treatment of IIIa in CH2Cl2 with urea chloride at room temp. Hydrogenation of 1.86 g VIII in methanolic HCl yielded 1.25 g H-Tyr-(AC)-OMe.HCl (IX), m. 214.5-15.5.degree. (decompn.). IX (0.82 g) and 1.43 g Z-Phe-OTCP (X) in 50 ml DMF with 0.43 ml Et3N gave 1.03 g Z-Phe-Tyr-(AC)-OMe (XI), m. 187-8.degree. (MeOH). XI (0.52 g) in 4 ml Me2NAc with 0.32 ml N2H4.H2O gave 0.28 g Z-Phe-Tyr-NHNH2 (XII), m. 224.5-25.degree. (decompn.). Heating 3.29 g IIIa and 10 ml iso-BuNCO at 60.degree. gave 3.28 g Z-Tyr-(BAC)-OMe, m. 108.5.degree. (CHCl3-ligroine), converted into H-Tyr-(BAC)-OMe.HBr, (XIII), m. 210.5-11.5.degree. (87.5%) by treatment

with HBr in AcOH. XIII (0.75 g), 0.95 g X, and 0.28 ml Et3N in 10 ml DMF gave 0.98 g Z-Phe-Tyr-(BAC)-OMe (XIV), m. 196-8.degree.. Hydrolysis of 0.58 g XIV in 7 ml Me2NAc and 5 ml dioxane with 1.5 ml 2N NaOH gave 0.36 g Z-Phe-Tyr-OH, m. 189-9.5.degree.. Treatment of XIII with N2H4.H2O in Me2NAc at room temp. gave 88% XII. Similarly prepd. were: Z-Tyr-(PAC)-OMe, m. 140-1.degree.; H-Tyr-(PAC)-OMe.HBr, m. 205.5.degree. (decompn.); Z-Phe-Tyr-(PAC)-OMe, m. 193-5.degree. (CHCl3-petroleum ether); Z-Phe-Tyr-OMe, m. 143-4.degree.. Stirring 60 g tyrosine benzyl ester with BOC-azide in C5H5N gave 62.5 g BOC-Tyr-OCH2Ph, m. 126-7.degree., which with PhNCO in DMF at room temp. gave 72% BOC-Tyr-(PAC)-OCH2Ph (XV), m. 108-8.5.degree. (aq. EtOH). Hydrogenation of XV in MeOH gave 84% BOC-Tyr-(PAC)-OH, m. 125-30.degree. (AcOEt-petroleum ether), from which were prepd. BOC-Tyr-(PAC)-OTCP, m. 162.degree. (iso-PrOH); BOC-Tyr-(PAC)-Phe-OMe, m. 152-3.degree. (sintering from 115.degree.); BOC-Tyr-Phe-NHNH2, m. 208.degree.. Also prepd. was Z-Tyr-(NPAC)-OMe (from IIIa and 4-O2NC6H4NCO), m. 179-80.degree., after chromatog.

IT **19391-47-0P 19391-48-1P 19391-49-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

L15 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1968:467676 HCAPLUS
DOCUMENT NUMBER: 69:67676
TITLE: Peptide syntheses with O-carbamoyltyrosine derivatives
AUTHOR(S): Jaeger, Georg; Geiger, Rolf; Siedel, Walter
CORPORATE SOURCE: Farbwerke Hoechst A.-G., Frankfurt/M., Fed. Rep. Ger.
SOURCE: Chemische Berichte (1968), 101(8), 2762-70
CODEN: CHBEAM; ISSN: 0009-2940
DOCUMENT TYPE: Journal
LANGUAGE: German
OTHER SOURCE(S): CASREACT 69:67676

AB The carbamoyl residue was used as an O-protective group for tyrosine. It could be removed with nucleophilic reagents, but was stable to proton solvolysis and hydrogenolysis. In peptide synthesis the carbamoyl protective group is not attacked by the amino component.

IT **19391-47-0P 19391-48-1P 19391-49-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

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FILE LAST UPDATED: 01 May 1997 (19970501/UP)

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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   21 APR 2004  HIGHEST RN 676437-01-7
DICTIONARY FILE UPDATES:  21 APR 2004  HIGHEST RN 676437-01-7

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

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  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

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L14  ANSWER 1 OF 7  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   123375-14-4  REGISTRY
CN   L-Tyrosine, N-[O-(aminocarbonyl)-N-[(phenylmethoxy)carbonyl]-L-tyrosyl]-,
     ethyl ester, carbamate (ester), homopolymer (9CI)  (CA INDEX NAME)
FS   STEREOSEARCH
MF   (C30 H32 N4 O9)x
CI   PMS
PCT  Polyamide, Polyamide formed
SR   CA
LC   STN Files:   CA, CAPLUS, USPATFULL

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     CRN  123375-13-3
     CMF  C30 H32 N4 O9

Absolute stereochemistry.
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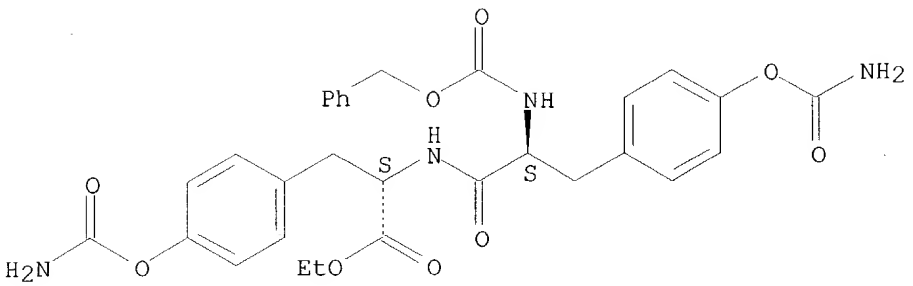
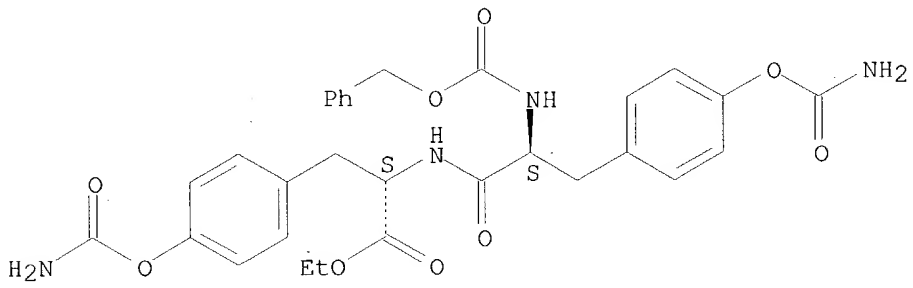


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 111:195409

L14 ANSWER 2 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN 123375-13-3 REGISTRY
CN L-Tyrosine, N-[O-(aminocarbonyl)-N-[(phenylmethoxy)carbonyl]-L-tyrosyl]-, ethyl ester, carbamate (ester) (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C30 H32 N4 O9
CI COM
SR CA

Absolute stereochemistry.



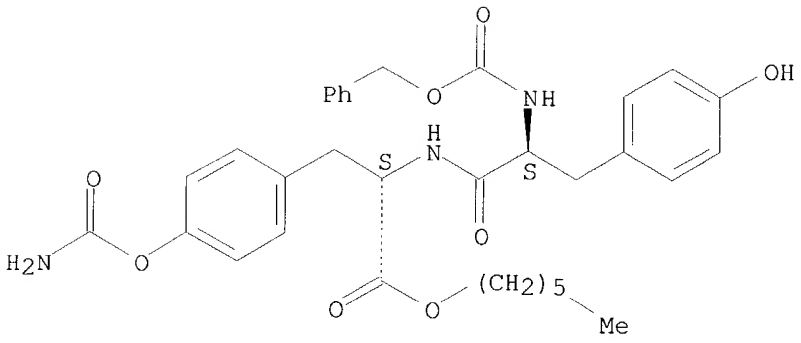
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L14 ANSWER 3 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN 106231-87-2 REGISTRY
CN L-Tyrosine, N-[N-[(phenylmethoxy)carbonyl]-L-tyrosyl]-, hexyl ester, 4-carbamate, homopolymer (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF (C33 H39 N3 O8)x
CI PMS
PCT Polyamide, Polyamide formed
SR CA
LC STN Files: CA, CAPLUS, CASREACT, TOXCENTER

CM 1

CRN 106231-86-1
CMF C33 H39 N3 O8

Absolute stereochemistry.



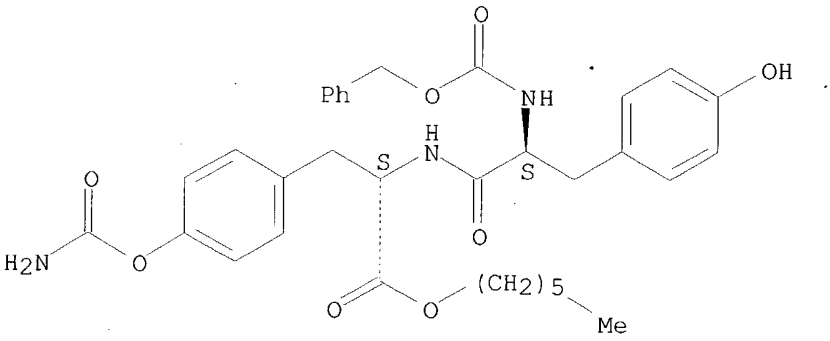
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 113:178192

REFERENCE 2: 106:67663

L14 ANSWER 4 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN 106231-86-1 REGISTRY
CN L-Tyrosine, N-[N-[(phenylmethoxy)carbonyl]-L-tyrosyl]-, hexyl ester, 4-carbamate (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C33 H39 N3 O8
CI COM
SR CA

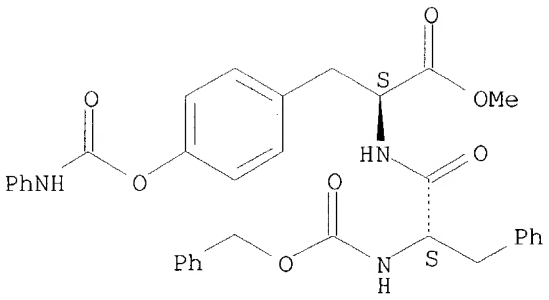
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L14 ANSWER 5 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN 19391-49-2 REGISTRY
CN Tyrosine, N-(N-carboxy-3-phenyl-L-alanyl)-, N-benzyl methyl ester, carbanilate (ester), L- (8CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C34 H33 N3 O7
LC STN Files: BEILSTEIN*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

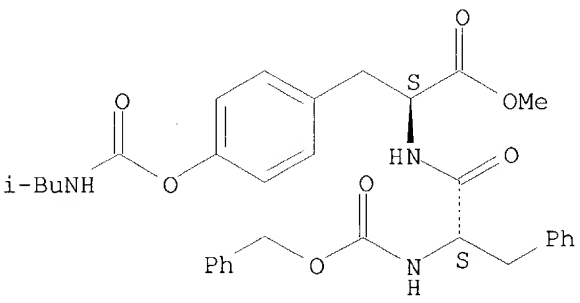
2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 73:110135

REFERENCE 2: 69:67676

L14 ANSWER 6 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN 19391-48-1 REGISTRY
CN Tyrosine, N-(N-carboxy-3-phenyl-L-alanyl)-, N-benzyl methyl ester, isobutylcarbamate (ester), L- (8CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Carbamic acid, isobutyl-, ester with N-(N-carboxy-3-phenyl-L-alanyl)-L-tyrosine N-benzyl methyl ester (8CI)
FS STEREOSEARCH
MF C32 H37 N3 O7
LC STN Files: BEILSTEIN*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

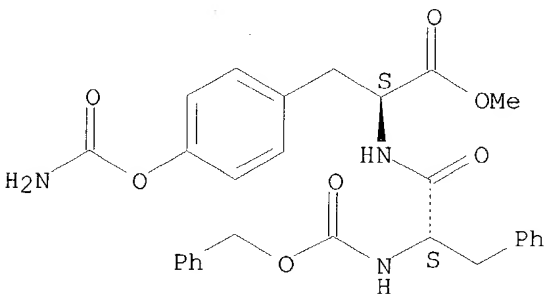
REFERENCE 1: 73:110135

REFERENCE 2: 69:67676

L14 ANSWER 7 OF 7 REGISTRY COPYRIGHT 2004 ACS on STN
RN 19391-47-0 REGISTRY

CN Tyrosine, N-(N-carboxy-3-phenyl-L-alanyl)-, N-benzyl methyl ester, carbamate (ester), L- (8CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H29 N3 O7
LC STN Files: BEILSTEIN*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB
(*File contains numerically searchable property data)

Absolute stereochemistry.



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REFERENCE 1: 73:110135

REFERENCE 2: 69:67676